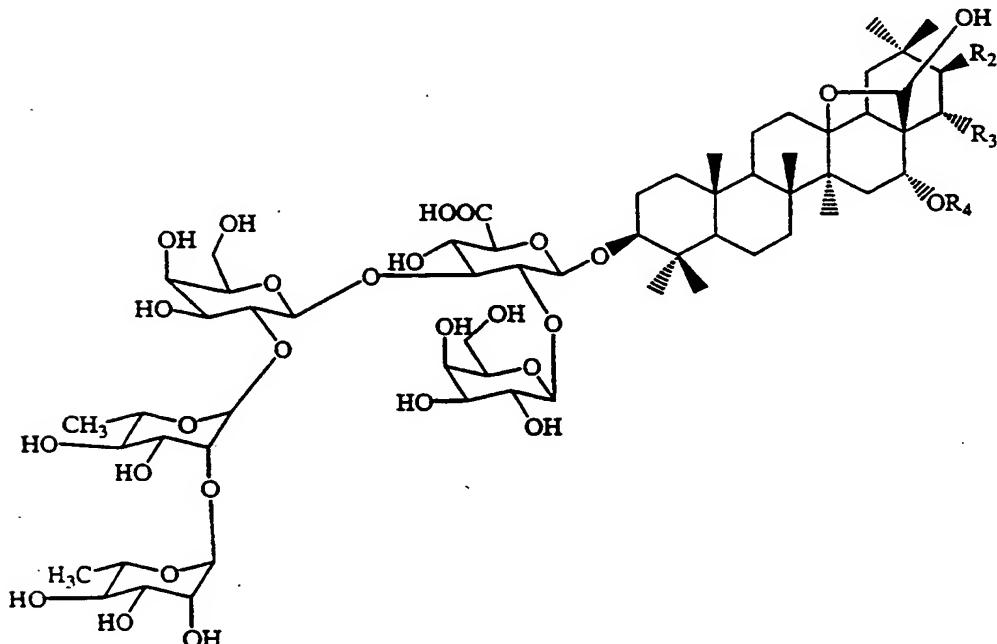


Claims

1. A process for the isolation of triterpene saponins from plants belonging to the family *Myrsinaceae*, characterized in that said process comprises the steps of
 - (a) extracting the dried plant parts with an alcohol and concentrating the extract,
 - (b) removing the apolar fraction from the extract by liquid-liquid extraction with an apolar solvent, and
 - (c) further purifying the saponins in the alcohol extract by liquid -liquid extraction, filtration and chromatography.
- 10 2. A process according to claim 1 wherein the alcohol is methanol, ethanol, isopropanol, butanol, each optionally admixed with water.
3. A process according to claim 1 wherein the saponins of the alcohol extract are further purified by
 - (c6) extracting the aqueous fraction with butanol saturated with water,
 - (c7) evaporating the organic layer to dryness,
 - (c8) washing the residue in a ketone, and
 - (c9) filtering off the crude saponin mixture.
- 20 4. A process according to claim 1 wherein the saponins are isolated from the plant species *Maesa balansae*, and the chromatography comprises straight phase chromatography/liquid chromatography on silicagel or reversed-phase liquid chromatography with gradient eluent system using
 - A : 0.5 % ammonium acetate in water
 - B : methanol
 - C : acetonitrilewherein at t = 0, (A:B:C) = (60:20:20) and t = end, (A:B:C) = (0:50:50).
- 30 5. A triterpene saponin obtainable by a process according to anyone of claims 1 to 4.
6. A triterpene saponin according to claim 5 wherein said saponin is isolated from the plant species *Maesa balansae*, and the chromatography comprises reversed-phase liquid chromatography with gradient eluent system using
 - A : 0.5 % ammonium acetate in water
 - B : methanol
 - C : acetonitrilewherein at t = 0, (A:B:C) = (60:20:20) and t = end, (A:B:C) = (0:50:50), and wherein said saponin has the following characteristics :

Compound 1 : MW = 1532, λ_{\max} = 228.6 nm, $\lambda_{\max 2}$ = 273.3 nm ;
 Compound 2 : MW = 1510, λ_{\max} = 223.9 nm, $\lambda_{\max 2}$ = 274.5 nm ;
 Compound 3 : MW = 1532, λ_{\max} = 279.2 nm, $\lambda_{\max 2}$ = 223.9 nm ;
 Compound 4 : MW = 1510, λ_{\max} = 280.4 nm, $\lambda_{\max 2}$ = 222.7 nm ;
 5 Compound 5 : MW = 1574, λ_{\max} = 276.8 nm, $\lambda_{\max 2}$ = 225.0 nm ; or
 Compound 6 : MW = 1552, λ_{\max} = 279.2 nm, $\lambda_{\max 2}$ = 223.9 nm.

7. A triterpene saponin having the formula



10 wherein R₂ is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ or $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R₃ is (E) or (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$, and
 R₄ is hydrogen or $-(\text{C}=\text{O})\text{CH}_3$.

15 8. A compound according to claim 7 wherein
 in compound 1, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 R₃ is (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,
 R₄ is hydrogen;
 in compound 2, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R₃ is (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,
 20 R₄ is hydrogen;
 in compound 3, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 R₃ is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,
 R₄ is hydrogen;

in compound 4, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,

R₃ is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,

R₄ is hydrogen;

in compound 5, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,

R₃ is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,

R₄ is $-(\text{C}=\text{O})\text{CH}_3$;

in compound 6, R₂ is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,

R₃ is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH-C}_6\text{H}_5$,

R₄ is $-(\text{C}=\text{O})\text{CH}_3$.

10

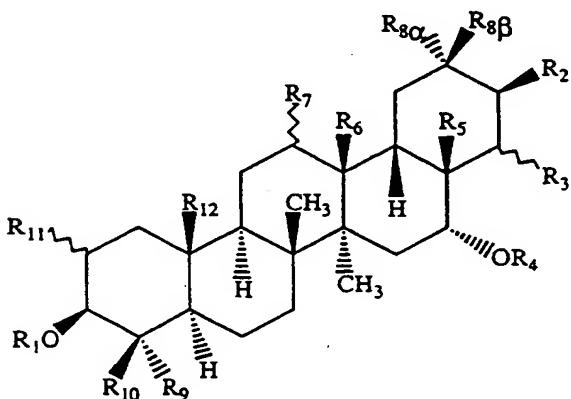
9. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and as an active ingredient a triterpene saponin as defined in claim 5, 6, 7 or 8.

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10. A composition according to claim 7 adapted for parenteral administration.

15

11. Use of one or more triterpene saponins for the preparation of a pharmaceutical composition for treating leishmaniasis in hosts infected by *Leishmania* species, characterized in that the saponin has the formula



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a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

R₁ is hydrogen, $-(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$, $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ substituted with phenyl, a monosaccharide group or an oligosaccharide group ;

R₂ is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ substituted with phenyl ;

R₃ is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ substituted with phenyl ;

25

R₄ is hydrogen, $\text{C}_{1.6}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$, $-(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ substituted with phenyl ;

R_5 is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $COOH$; or
 R_5 and R_2 form a divalent radical of formula $-C(=O)-O-$;
 R_6 and R_7 are hydrogen; or taken together they form a bond; or
 R_5 and R_6 form a divalent radical of formula

5 - CH_2-O- (a),
- $CH(OR_{13})-O-$ (b),
- $C(=O)-O-$ (c),

wherein R_{13} is hydrogen, C_{1-6} alkyl or $-(C=O)C_{1-5}$ alkyl ;

10 $R_{8\alpha}$ and $R_{8\beta}$ each independently represent CH_3 , CH_2OH , CH_2OCH_3 ,
 $CH_2O-C(=O)C_{1-5}$ alkyl, CHO , $CH(OCH_3)_2$, $CH=NOH$, $COOH$;
 $R_{8\beta}$ and R_3 form a divalent radical of formula $-C(=O)-O-$;
 $R_{8\beta}$ and R_5 form a divalent radical of formula $-CH_2O-CHOH-$;
 R_9 is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)C_{1-5}$ alkyl, CHO , $COOH$;
 R_{10} is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)C_{1-5}$ alkyl, CHO , $COOH$;
15 R_{11} is hydrogen, hydroxy or $O-C(=O)C_{1-5}$ alkyl ; or R_{10} and R_{11} form a divalent
radical of formula $-CH_2O-$; and
 R_{12} is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $CH=NOH$, or $COOH$.

12. Use according to claim 11 wherein

20 R_1 is hydrogen, $-(C=O)C_{1-5}$ alkyl, or an oligosaccharide group ;
 R_3 is hydrogen, hydroxy, $-O(C=O)C_{1-5}$ alkyl, $-O(C=O)C_{2-5}$ alkenyl,
- $O(C=O)C_{2-5}$ alkenyl substituted with phenyl ;
 R_4 is hydrogen, C_{1-6} alkyl, $-(C=O)C_{1-5}$ alkyl, $-(C=O)C_{2-5}$ alkenyl ;
 R_5 is CH_2OH , $CH_2O-C(=O)CH_3$, CHO ; and
25 R_6 and R_7 taken together form a bond; or
 R_5 and R_6 form a divalent radical of formula

- CH_2-O- (a),
- $CH(OR_{13})-O-$ (b),
- $C(=O)-O-$ (c),

30 wherein R_{13} is hydrogen, C_{1-6} alkyl or $-(C=O)C_{1-5}$ alkyl, ; and

R_7 is hydrogen ;
 $R_{8\beta}$ represents CH_3 , CH_2OH , CHO , $CH(OCH_3)_2$, $CH=NOH$, $COOH$;
 $R_{8\alpha}$ represents CH_3 ;
 $R_{8\beta}$ and R_3 form a divalent radical of formula $-C(=O)-O-$; or
35 $R_{8\beta}$ and R_5 form a divalent radical of formula $-CH_2O-CHOH-$;
 R_{10} is CH_3 , CH_2OH ;
 R_{11} is hydrogen, hydroxy or $O-C(=O)C_{1-5}$ alkyl ; or

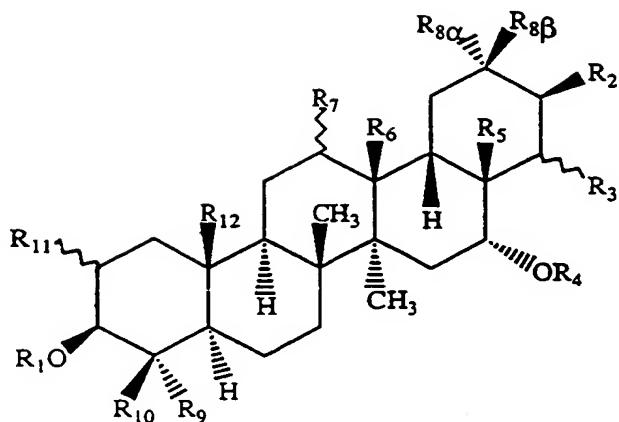
R₁₀ and R₁₁ form a divalent radical of formula -CH₂O- ; and R₁₂ is CH₃, CH₂OH, CH₂O-C(=O)CH₃, CHO, or CH=NOH.

13. Use according to claim 12 wherein

5 R₁ is hydrogen or an oligosaccharide group ;
R₂ is hydrogen, hydroxy, -O(C=O)C₁₋₅alkyl, -O(C=O)C₂₋₅alkenyl, -O(C=O)C₆H₅,
or -O(C=O)C₂₋₅alkenyl substituted with phenyl ;
R₃ is hydrogen, hydroxy, -O(C=O)C₁₋₅alkyl, -O(C=O)C₂₋₅alkenyl,
-O(C=O)C₂₋₅alkenyl substituted with phenyl ;
10 R₄ is hydrogen, C₁₋₆alkyl, -(C=O)C₁₋₅alkyl, -(C=O)C₂₋₅alkenyl, -(C=O)C₂₋₅alkenyl
substituted with phenyl ;
R₅ is CH₂OH, CH₂OCH₃, CH₂O-C(=O)CH₃, CHO, COOH ; and
R₆ and R₇ taken together form a bond; or
R₅ and R₆ form a divalent radical of formula
15 -CH₂-O- (a),
-CH(OR₁₃)-O- (b),
-C(=O)-O- (c),
wherein R₁₃ is hydrogen ; and
R₇ is hydrogen ;
20 R_{8 α} and R_{8 β} both represent CH₃ ;
R₉ is CH₃ ;
R₁₀ is CH₃ ;
R₁₁ is hydrogen ; and
R₁₂ is CH₃.

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14. A method of alleviating clinical manifestations of, and curing disorders known as leishmaniasis attributable to infection by protozoan parasites of the genus *Leishmania* in both men and animals, comprising administering to an infected host a therapeutically effective amount of a compound of formula:



a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

5 R_1 is hydrogen, $-(C=O)C_{1-5}alkyl$, $-(C=O)C_{2-5}alkenyl$, $-(C=O)C_{2-5}alkenyl$ substituted with phenyl, a monosaccharide group or an oligosaccharide group;

R₂ is hydrogen, hydroxy, -O(C=O)C₁₋₅alkyl, -O(C=O)C₂₋₅alkenyl, -O(C=O)C₆H₅, or -O(C=O)C₂₋₅alkenyl substituted with phenyl ;

R₃ is hydrogen, hydroxy, -O(C=O)C₁₋₅alkyl, -O(C=O)C₂₋₅alkenyl, -O(C=O)C₆H₅, or -O(C=O)C₂₋₅alkenyl substituted with phenyl :

10 R₄ is hydrogen, C₁₋₆alkyl, -(C=O)C₁₋₅alkyl, -(C=O)C₂₋₅alkenyl, -(C=O)C₆H₅, or -(C=O)C₂₋₅alkenyl substituted with phenyl :

R_5 is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $COOH$: or

R_1 and R_2 form a divalent radical of formula $-C(=O)-O-$:

R_6 and R_7 are hydrogen; or taken together they form a bond; or

15 R_5 and R_6 form a divalent radical of formula

-CH₂-O- (a),

$$-\text{CH}(\text{OR}_{13})-\text{O}- \quad (\text{b}).$$

$$-\text{C}(=\text{O})-\text{O}- \quad (\text{c}),$$

wherein R₁₃ is hydrogen, C₁₋₆alkyl or -(C=O)C₁₋₆alkyl:

20 R_{8a} and R_{8b} each independently represent CH_3 , CH_2OH , CH_2OCH_3 .

CH₂O-C(=O) C₁₋₅alkyl, CHO, CH(OCH₃)₂, CH=NOH, COOH;

R₈₈ and R₃ form a divalent radical of formula -C(=O)-O-;

R_{88} and R_5 form a divalent radical of formula $-CH_2O-CHOH-$;

R₉ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)C₁₋₅alkyl, CHO, COOH;

25 R₁₀ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)C₁₋₅alkyl, CHO, COOH;

R_{11} is hydrogen, hydroxy or $O-C(=O)C_{1-5}alkyl$; or R_{10} and R_{11} form a divalent radical of formula $-CH_2O-$; and

R_{12} is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $CH=NOH$, or $COOH$.